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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,385	ADAMOU ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *5-10,12-17,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11,18,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6903*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence search report (1)*.

DETAILED ACTION

Preliminary Amendment

1) Acknowledgment is made of Applicants' preliminary amendment filed 06/09/03. With this, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election, with traverse, of invention I, claims 1-4 and 11, filed 12/03/03, in response to the restriction requirement mailed 05/06/03. Applicants' traversal is on the grounds that an examination of invention I necessarily would involve the search of the vaccine of invention I, since a vaccine is only useful for treatment purposes. Applicants submit that claim 13, drawn to a method of use of the product of invention I, should be joined with invention I.

Applicants' arguments have been carefully considered. Since Applicants have elected the product of invention I, claims of invention III, drawn to a method of use of the product of invention I, would be kept pending pursuant to the rejoinder provisions of M.P.E.P 821.04, and would be rejoined with the elected product claims, if and when the latter were deemed allowable. *Process claims that depend from or otherwise include all the limitations of the patentable product* will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after the final rejection are governed by 37 C.F.R 1.116; amendments submitted after allowance are governed by 37 C.F.R 1.312. The requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103 and 112. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See 'Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C § 103(b),' 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicants are advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right rejoinder.

Numbering of Claims under 37 CFR 1.126

3) The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the

remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered second claim 21 (currently last claim) has been renumbered as claim 22.

Status of Claims

4) Claims 1-4 have been amended via the amendment filed 06/09/03.

New claims 18-21 and 21 (now renumbered and claim 22) have been added via the amendment filed 06/09/03.

Claims 1-22 are pending.

Claims 5-10, 12-17, 19 and 20 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

The elected claims 1-4 and 11 and the new claims 18, 21 and 22 are under examination.

Priority

5) The instant application is a divisional application of SN 09/590,991, filed 06/09/2000, now co-pending, which claims priority to the provisional application, SN 60/138,453, filed 06/10/1999.

Specification - Informalities

6) The instant specification is objected to for the following reason(s):

(a) The drawing 3 is objected to for lack of labeling of the two subparts or panels. The two panels of Figure 3 should be labeled as 3A and 3B. The figure description on page 5 of the specification should refer to the Figure as Figure 3A and 3B. Reference to these Figures throughout the specification should be amended accordingly.

(b) At line 13 on page 27, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

Rejection(s) under 35 U.S.C § 101

7) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

8) Claims 1-4, 18 and claims dependent therefrom are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

Instant claims do not sufficiently distinguish over a polypeptide or an immunogenic fragment thereof as it exists naturally, for example, on the surface of a microbe, or sloughed off the surface and being present in the nature, because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. The claims should be amended to indicate the hand of the inventor, e.g., by insertion of '--an isolated polypeptide ... --, or --a purified polypeptide-- if descriptive support exists for such a limitation in the instant application. See MPEP 2105.

Rejection(s) under 35 U.S.C § 112, First Paragraph

9) Claims 1-3 and11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that the polypeptide having an amino acid sequence that is at least 65%, 80% and 95% sequence identical to the amino acid sequence of SEQ ID NO: 8 (i.e., a polypeptide variant) as recited in the instant claims does not exist independent of its function, i.e., the ability to bind to antibody specific for *Streptococcus pneumoniae*. The specification discloses diagnostic applications or vaccine intentions for the claimed polypeptide variant. However, the instant specification fails to teach a single 'variant' having 65-80% sequence identity to the amino acid sequence of SEQ ID NO: 8 or an 'immunogenic fragment' thereof, which concurrently has the ability to bind to a *Pneumococcus*-specific antibody. Diagnostic or vaccine applications minimally require an ability to elicit a specific immune response or bind specifically to an antibody. The precise structure or relevant identifying characteristics of each DNA molecule that encodes a 'variant' polypeptide of SEQ ID NO: 8 having the specific binding ability can only be determined empirically by actually making every DNA molecule that encodes the polypeptide variant, and testing each varied DNA molecule to determine whether it encodes the recited polypeptide variant having the particularly disclosed specific binding activity. The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

A mere statement that the invention includes a polypeptide variant having 65-80% sequence identity to

the amino acid sequence of SEQ ID NO: 8 is insufficient to meet the adequate written description requirement of the claimed invention. The polypeptide of SEQ ID NO: 8 has specific biologic properties dictated by the structure of the protein and the corresponding structure of the structural gene sequence, which encodes it. A convincing structure-function relationship has to exist between the structure of the gene sequence, the structure of the polypeptide encoded, and the function of the encoded polypeptide. The function cannot be predicted from the modification of the structure of the gene and in the instant case, the DNA encoding the recited polypeptide variant. Applicants have not shown that variation or modification of a reference sequence encoding a reference protein as claimed would automatically predict the production of a protein variant having the recited functional activity, i.e., ability to bind to an antibody specific to *Streptococcus pneumoniae*. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of DNA molecules encoding a representative number of species of polypeptide variants of SEQ ID NO: 8 as recited, sufficient to allow one skilled in the art to determine that the inventors had possession of the invention as claimed. With the exception of a pneumococcal polypeptide of SEQ ID NO: 8, a skilled artisan cannot envision the detailed chemical structure of all the polypeptide variant species encompassed by the recited molecule. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. The nucleic acid encoding the polypeptide variant or an immunogenic fragment itself is required. See *Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.*

10) Claims 1-4, 11, 21 and 22 are rejected under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for an immunogenic composition or a vaccine containing a purified serotype 4 (Norway strain) *S. pneumoniae* polypeptide comprising the amino acid sequence of SEQ ID NO: 8 and a pharmaceutically acceptable carrier, wherein the polypeptide is present in an amount effective to elicit protective antibodies in a mammalian animal against challenge with a serotype 6B isolate of *S. pneumoniae,* does not reasonably provide enablement for a polypeptide comprising an amino acid sequence having at least 65% to 95% identity to SEQ ID NO: 8 (i.e., polypeptide variant) and a pharmaceutically acceptable carrier, wherein the polypeptide variant is present in an amount effective to elicit protective antibodies in any animal against challenge with any 'organism' of the genus *Streptococcus*, or any species or serotype of *S. pneumoniae* and a vaccine comprising the same, or for a vaccine comprising one or more immunogenic fragments of SEQ ID NO: 8 as recited in claims 21 and 22.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue

experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Instant claims encompass a polypeptide comprising an amino acid sequence having 65%, 80% or 95% identity to the amino acid sequence as shown in SEQ ID NO: 8, immunogenic fragments thereof (claims 1-4), and a vaccine comprising one or more of the same (claim 11). Claims 21 and 22 encompass a vaccine comprising specific fragments of SEQ ID NO: 8. However, the instant specification does not provide enablement for such polypeptide variants or truncated polypeptides, both functional as recited, and a vaccine comprising one or more of the same. There is no evidence within the instant specification to show that a polypeptide having an amino acid sequence that is 65%, 80% or 95% identical to the amino acid sequence of SEQ ID NO: 8, alone or in any combination, does have the ability to bind to an antibody specific for *Streptococcus pneumoniae*, does have the ability to serve as a vaccine, and is able to elicit 'protective' antibodies in an animal against 'an organism' of the whole genus *Streptococcus*. Further, there is no evidence that the specific truncated polypeptides have the ability to serve as a 'vaccine'. This is important because although the claimed polypeptide is said to have 65%, 80% or 95% identity with SEQ ID NO: 8, there is a 35%, 20% and 5% dissimilarity between SEQ ID NO: 8 and the claimed polypeptide variants, and the effects of these dissimilarities upon protein structure and function cannot be predicted. Although a microbial polypeptide or protein is expected in the art to generally induce specific antibodies, the ability of polypeptide variants and fragments of such variants to serve as a vaccine and confer protective immunity against a microbial disease, any streptococcal disease in the instant case, is not predictable. The instant specification provides no guidance as to which specific amino acids must be retained in the polypeptide variant or fragment and which may be varied or deleted without causing any detrimental effect to the claimed product that is meant for inducing an immune response in an animal. There is no guidance in the instant specification with regard to which amino acid variations, i.e., insertions, deletions, additions and substitutions, in the protein would result in a variant of SEQ ID NO: 8 or a fragment thereof that would retain the functional integrity or biological, antigenic and immunogenic competence of the native polypeptide of SEQ ID NO: 8, without rendering it non-functional. This is

important because the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. While it is known in the art that variation in one or more amino acids is possible in a given protein, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the protein's functional competence, is not predictable. For instance, Bowie *et al.* (*Science* 247: 1306-1310, 1990 – Applicants' IDS) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Bowie *et al.* further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (see column 1 on page 1306). Bowie *et al.* also teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (see column 2 on page 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess *et al.* (*J. Cell Biol.* 111: 2129-2138, 1990 – Applicants' IDS) who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similar teachings are provided by Lazar *et al.* (*Mol. Cellular Biol.* 1988, 8: 1247-1252), who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. All these references demonstrate that even a single amino acid substitution/deletion will often dramatically affect the biological activity and characteristics of a protein. Clearly, with 35%, 20% or 5% dissimilarity to the polypeptide of SEQ ID NO: 8, the function of the claimed polypeptide variants could not be predicted, based on the sequence similarity or identity with SEQ ID NO: 8, nor would it be expected to be the same as that of the polypeptide of SEQ ID NO: 8. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and specific binding property of the protein, would result in a polypeptide that may be non-functional, or not optimally antigenic as a diagnostic reagent, or not optimally immunogenic as a vaccine candidate, because such positions tolerate no or little modifications. For instance, Houghten *et al.* (New Approaches to Immunization, *Vaccines86*,

Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten *et al.* state (see page 24):

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide, which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism. In the instant case, this is important because one of the purposes of the instant invention is to produce a polypeptide variant or a fragment of the recited SEQ ID NO: 8 in its biologically active, immunogenic and/or protective form for inducing a *Pneumococcus*-specific immune response. The instant disclosure lacks guidance on the precise position(s), nature and extent of amino acid replacements, deletions or variations that can be made in the claimed protein or polypeptide in order to produce a polypeptide variant or fragment, and with regard to whether it would serve as an effective vaccine capable of conferring immunity against any streptococcal disease. It is emphasized that predictability or unpredictability is one of the *Wands* factors for enablement. There appears to be no evidence that the claimed variants and fragments were indeed made and tested for their ability to serve as an effective vaccine composition by any acceptable animal model. Absent a concrete showing that the claimed polypeptide variants and fragments thereof are effective in protecting against any streptococcal infections, or eliminate or reduce morbidity and/or mortality due to such infections, the claims are considered as being non-enabled. The same is true with the protective ability of the specific fragments of SEQ ID NO: 8. Clearly, the specification lacks adequate guidance and disclosure that would limit the experimentation from being undue. Given the art-recognized unpredictability associated with the structure-function relationship of a varied or truncated protein or polypeptide, one of skill in the art would look into the specification for specific teaching and guidance, which in the instant case is lacking. Due to the lack of specific guidance and disclosure as to the precise structure of the polypeptide variants and fragments that are functional and *Pneumococcus*-specific; the lack of demonstration of their antigenic, immunogenic, diagnostic and protective ability; the lack of working examples enabling the full scope of the claims; the art-recognized unpredictability factor associated with the functions of a polypeptide following variation or deletion; the breadth of the claims; and the quantity of experimentation necessary, undue experimentation would have been required to practice the invention as claimed. *Ex parte*

Foreman, 230 USPO 546, 547 (*Bd. Pat. Appeals. and Inter.* 1986). The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C. § 112, first paragraph.

11) Claim 11 is rejected under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for a vaccine containing a purified serotype 4 (Norway strain) *S. pneumoniae* polypeptide comprising the amino acid sequence of SEQ ID NO: 8 and a pharmaceutically acceptable carrier, wherein the polypeptide is present in an amount effective to elicit protective antibodies in a mammalian animal against challenge with a strain of serotype 6B of *S. pneumoniae,* does not reasonably provide enablement for such a vaccine comprising a polypeptide comprising the amino acid sequence of SEQ ID NO: 8 and a pharmaceutically acceptable carrier, wherein the polypeptide is present in an amount effective to elicit protective antibodies in any animal against challenge with any 'organism' of the genus *Streptococcus*, any species of the genus *Streptococcus*, or any serotype of *S. pneumoniae* other than serotype 6B.

The instant claim is evaluated based on the *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the claimed vaccine is related to one or more polypeptide variants of SEQ ID NO: 8 having at least 65-95% sequence identity with SEQ ID NO: 8 from a specific serotype of *S. pneumoniae*, i.e., serotype 4 or Norway 4, which induces protective antibodies in an animal against 'an organism of the genus *Streptococcus*'. However, the scope of the claim broadly encompasses elicitation of protective antibodies by the polypeptide or its variant(s) in any animal against any organism of the genus *Streptococcus*. The generic limitation 'animal' in the claim encompasses an animal that is vertebrate, non-vertebrate, mammalian, non-mammalian, multicellular, transgenic etc. The limitation, "an organism of the genus *Streptococcus*" appears to encompass multiple species of *Streptococcus*, such as, *S. pyogenes, S. mutans, S. viridans, S. agalactiae etc.*, and multiple serotypes of *Streptococcus,* including 23 serotypes of *S. pneumoniae,* and those *Streptococci* yet to be discovered. The instant specification, for example at Figure 1, shows that a vaccine comprising an effective amount of a polypeptide comprising an amino acid sequence that is 100% identical to SEQ ID NO: 8 of serotype 4 (Norway strain) *S.*

pneumoniae and a pharmaceutically acceptable carrier, elicits protective antibodies in a mammalian animal against challenge with a serotype 6B *S. pneumoniae,* strain SJ2. However, there is no evidence within the instant specification showing that one or more polypeptide variants of SEQ ID NO: 8 as recited, from serotype 4 of *S. pneumoniae*, or a non-serotype 4 *S. pneumoniae,* would indeed elicit "protective" antibodies in any animal against any species of the genus *Streptococcus* other than *S. pneumoniae*, or any serotype of *S. pneumoniae* other than the serotype 6B. There is no showing that the claimed polypeptide variants are immunologically or biologically specific and effective against all species of the genus *Streptococcus*, or all 23 serotypes of S. *pneumoniae* that are known thus far, and those yet to be discovered. This is important because the ability of a microbial polypeptide or its variants obtained from one serotype of that microbe to confer a broad genus-wide, species-wide, or serotype-wide protection is not predictable. There is no evidence within the instant specification that the polypeptide of SEQ ID NO: 8 is produced by all members or species of the genus *Streptococcus,* or by all serotypes of *S. pneumoniae* other than serotype 4, and that it confers homologous and heterologous protection against any member of the genus *Streptococcus* or any *S. pneumoniae* other than serotype 6B. The evidence is clearly not commensurate in scope with the breadth of the claim(s). Absent concrete evidence showing that the claimed polypeptide (or its variants as claimed) is produced by all serotypes of *Streptococcus pneumoniae* and that it confers homologous and heterologous protection against any member of the genus *Streptococcus,* or any serotype of *S. pneumoniae* other than 6B, claim 11 is viewed as being non-enabled with respect to its full scope.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

12) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

13) Claims 1-4, 11, 18, 21 and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 11 is vague, indefinite and confusing in the recitation 'organism of the genus *Streptococcus*'. The term 'organism' is much broader than the term 'the genus *Streptococcus*'. The limitation 'organism' encompasses humans, non-humans, viruses, fungi, parasites, bacteria etc. whereas '*Streptococcus*' represents the much narrower bacterial genus, which constitutes a much smaller species within the genus organism. Does the term 'organism' in the claim represent an isolate, strain or a species

of the genus *Streptococcus*?

(b) Claim 1 is confusing in the recitation 'composition comprising a polypeptide, including immunogenic fragments thereof'. It is unclear whether the claimed composition: a) comprises a polypeptide that is 65% identical to SEQ ID NO: 8, or such a polypeptide plus immunogenic fragments thereof; or b) whether the polypeptide comprises within it immunogenic fragments. Clarification/correction is requested.

(c) Analogous criticism applies to claim 18.

(d) Claim 11 has improper antecedence for the recitation 'said polypeptide' (see line 5), because the earlier recitation in the claim is of 'polypeptides' [Emphasis added].

(e) Claim 22 has improper antecedence for the recitation 'said immunogenic fragment' (see line 1). Claim 22 depends from claim 18, which recites 'immunogenic fragments', but not an 'immunogenic fragment' [Emphasis added].

(f) Claim 21 is indefinite and confusing in the limitation: 'said immunogenic fragments comprise one or more of the fragments'. The term 'fragments' necessarily has to include more than 'one' fragment, and cannot have 'one' fragment as recited.

(g) Claim 11 is confusing and/or lacks proper antecedent basis for the recitation: "*S. pneumoniae* polypeptides selected from the group consisting of the polypeptides of claims 1, 2, 3 and 4". Claim 11 depends from claim 1, 2, 3 or 4, which does not refer to the polypeptides as "*S. pneumoniae* polypeptides".

(h) Claims 21 and 22 are vague and indefinite in that these claims fail to distinctly identify 'SEQ ID NO: 8' as the amino acid sequence. For clarity and for consistency with the claim language used in claims 1, 4 and 18, it is suggested that Applicants replace the recitation 'of SEQ ID NO: 8' with --of the amino acid sequence of SEQ ID NO: 8--.

(i) Claims 2-4, 11, 21 and 22, which depend directly or indirectly from claim 1 or claim 18, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

14) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15) Claims 21 and 22 are rejected under 35 U.S.C § 102(b) as being anticipated by Choi *et al.* (WO 98/18930 A2 – Applicants' IDS) ('930).

The term "vaccine" in the instant claims is viewed as the intended use of the product.

Choi *et al.* ('930) disclosed a polypeptide from *Streptococcus pneumoniae* which includes the fragment comprising amino acid residues 657-773 of the instantly recited SEQ ID NO: 8, and a vaccine comprising the same and a pharmaceutically acceptable carrier for inducing protective antibodies against *Streptococcus pneumoniae*. See the enclosed sequence search report and pages 4 and 62, SEQ ID NO. 68 in Table 1 of Choi *et al.* That an amino acid sequence which is 657-773 residues-long is intrinsically immunogenic is inherent from the teachings of Choi *et al.*

Claims 21 and 22 are anticipated by Choi *et al.* ('930).

Remarks

16) Claims 1-4, 11, 18, 21 and 22 stand rejected.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

18) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER